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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,438	07/13/2004	Andras Bertha	BERTHA-4	9435

545 7590 01/18/2006

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EXAMINER	
KOSSON, ROSANNE	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 01/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,438	BERTHA, ANDRAS	
	Examiner	Art Unit	
	Rosanne Kosson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) *1 and 2* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 3-5, in the reply filed on December 1, 2005 is acknowledged. Claims 1-2 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. No claims have been amended, canceled or added. Accordingly, claims 3-5 are examined on the merits herewith.

Applicant has traversed the restriction requirement, asserting that the two inventions are related to a similar inventive concept, because they are both related to obtaining anti-tumor substances from gestating or lactating even-toed mammals having leukosis and because concentrations of immune cell components are high in the blood in the colostrum of these animals. In reply, the instant application claims two different methods, each with a different set of steps applied to a different starting material, for obtaining an anti-tumor substance. As discussed in the restriction requirement Office action, the two inventions do not share a special corresponding technical feature, particularly as the anti-tumor substance is not a defined substance. The instant application claims two different methods of preparing an animal extract that has anti-tumor properties. That both methods are related to a similar concept does not provide unity of invention. Further, the concepts of gestating or lactating mammals and blood or colostrum that has a high concentration of immune cell components are not limitations

recited in the claims. Because unity of invention is lacking, the restriction requirement is maintained and is made final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 4-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of obtaining an anti-tumor substance from the colostrum of even-toed hoofed animals with leukosis, in which the method recites specific time periods for performing each part of each step, such as centrifugation times and time periods for shaking colostrum, or a colostrum fraction with an organic solvent mixture, does not reasonably provide enablement for a method of obtaining an anti-tumor substance from the colostrum of even-toed hoofed animals with leukosis, in which the method recites no specific time periods for performing the various operations required. Also not enabled are method steps that recite diluting the freeze-dried floating upper layer fraction and the freeze-dried medial crust layer to any concentration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether or not undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd

1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue

experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

The claims are very broad because they recite, in steps without specific parameters, a method of obtaining an anti-tumor substance from the colostrum of even-toed hoofed animals with leukosis. The substance is undefined.

2. The nature of the invention.

The invention is designed to provide an animal extract that has anti-tumor properties.

3. The state of prior art.

As discussed below, Janusz et al. (US 2005/0152985) disclose that mammalian colostrum contains the polypeptide colostrinin, which has a number of biological activities, including stimulating the release of cytokines from lymphocytes (see paragraphs 1-3, 6, 7 and 44). Cytokines have anti-cancer properties and are

administered to cancer patients (see Cancer Principles & Practice of Oncology, 6th Ed., De Vita et al., eds., Lippincott Williams & Wilkins, Philadelphia, 2001, pp. 308-312). Thus, it was known at the time of Applicant's invention that colostrum has anti-cancer properties. One of ordinary skill in the art would have expected these anti-cancer properties in colostrum from normal mammals and from animals with leucosis.

4. The relative skill in the art.

The relative skill in the art as it relates to the method of the invention is characterized by that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

As noted above, the anti-tumor substance of Janusz et al. is the polypeptide colostrinin. But, this may or may not be Applicant's anti-tumor substance. Applicant has not disclosed what the anti-tumor substance is. Thus, one of skill in the art, while performing the claimed method, cannot test for the presence of the anti-tumor substance in a quantitative or qualitative manner at various stages in the purification procedure to determine how much of the anti-tumor substance is present at each stage. The incomplete steps in the claimed method do not permit one of skill in the art to prepare positive and negative controls. Thus, while performing the claimed method, one of skill in the art cannot determine whether or not each step has been successfully performed. Because the anti-tumor substance is not known, one of skill in the art cannot develop an assay for the anti-tumor substance. Further, the claimed steps do not provide enough information for one of skill in the art to carry out a method of obtaining an anti-tumor substance from the colostrum of an even-toed hoofed animal

having leukosis. Steps a) and c) recite shaking colostrum or a colostrum fraction with a 1:1 mixture of isopropyl alcohol and chloroform, but one of skill in the art would not know how long to shake the colostrum-solvent mixture so that the anti-tumor substance can eventually be isolated. Similarly, steps b) and e) recite centrifuging the shaken mixture at a speed of at least 5000 rpm for an indefinite period of time in a cooled state. One of ordinary skill in the art would not know how long this mixture must be centrifuged so that the anti-tumor substance can eventually be isolated. In step 4f) and in claim 5, the freeze-dried upper layer and crust layer are diluted in physiological saline solution, but one of skill in the art would not know how much to dilute these freeze-dried fractions (freeze-dried and presumably redissolved, as only liquids but not solids can be diluted) so that an anti-tumor substance is obtained. Because the substance itself is not disclosed, and therefore cannot be assayed for, as one cannot develop an assay for an unknown substance (no assay for colostrum and its fractions is disclosed either), one of skill in the art requires complete method steps, i.e., with shaking times, centrifugation times and dilution ratios, in order to carry out the claimed method. Practicing the method as claimed, it cannot be predicted that one of skill in the art will isolate an anti-tumor substance from the starting colostrum. Although the prior art discloses an anti-tumor substance in the colostrum of even-toed hoofed animals, it is not obtained by the method in Applicants' specification, a portion of which is recited in the instant claims. Thus, the prior art does not allow one to predict that one of skill in the art can isolate an anti-tumor substance from the starting colostrum by practicing the method as claimed.

6. The amount of guidance present.

As discussed above, guidance for obtaining an anti-tumor substance from the colostrum of even-toed hoofed animals with leukosis is provided on pp. 2-3 of the specification. But, these steps are not recited completely in the claims. Regarding steps 4a) and 4c), the specification discloses that shaking times of eight minutes are required. Regarding steps 4b) and 4e), the specification discloses that centrifugation times of 20 minutes are required. The specification does not disclose ranges or minimal times. Regarding the dilution factor in step 4f) and in claim 5, the specification discloses on p. 3 that favorable experimental results were obtained with the diluted anti-tumor substance. Thus, a therapeutically effective dose is used. A range of dilution factors is not provided, and any dilution ratio is not necessarily therapeutically effective.

7. The existence of working examples.

The guidance discussed above is a working example, although not specifically labeled as such. Nevertheless, as discussed above, the working example provides one shaking time, one centrifugation time, and one dilution ratio. Ranges and minima for these parameters are not provided in the specification.

8. The quantity of experimentation necessary.

To prove that an anti-tumor substance may be isolated from the colostrum of an even-toed hoofed animal having leukosis by a method in which any shaking time may be used, after combining the colostrum, or a fraction of the colostrum, with an organic solvent mixture, or in which the colostrum-solvent mixture may be centrifuged for any length of time, or in which the resulting freeze-dried fractions may be diluted to any degree, many experiments would have to be conducted under a wide range of

conditions. In these experiments, many shaking times would have to be tested, each with a different centrifugation time in the centrifugation steps. Conversely, many centrifugation times would have to be tested, each with a different shaking time in the shaking steps. For each pair of shaking time and centrifugation time, a number of freeze-dried fractions would have to be prepared and each one diluted to a different degree to determine which final diluted fractions have anti-tumor properties. An assay would have to be developed for the many intermediate and final fractions obtained, but, because the substance is not defined, an assay cannot be developed. Because the method steps are incomplete, positive and negative controls cannot be prepared, a further hindrance to developing an assay. The results of these experiments would have to show that whatever shaking times, centrifugation times and dilution ratios are used, the extract obtained has anti-tumor properties, which is not possible without a controlled assay.

These types of experiment and data are missing from the specification. A great deal of guidance is needed to establish the claimed method because the claims recite a method of obtaining an anti-tumor substance from the colostrum of even-toed hoofed animals having leukosis in which the method may be carried out with any shaking times, centrifugation times and dilution ratios for the freeze-dried products obtained. Even if the method may be carried out with one set of these parameters, without a very large amount of data, such a result could not be expected if any one of these parameters is changed, such as one or both of the centrifugation times or one of the dilution ratios.

Therefore, the claims fail to satisfy the enablement requirement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. For example, claim 3 recites the phrase "characterized in that said substance being taken from the colostrum of the animal." Claim 4, step a) recites "shaken with a 1:1 mixture of i-propyl alcohol and chloroform of identical volume on room temperature through a pre-determined period of time." Step e) recites that the organic phase is spilled. Additionally, the method steps use the passive voice- the colostrum is shaken, the material is centrifuged, etc.- rather than the more standard, active voice- shaking the colostrum, centrifuging the material, etc. Appropriate correction is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 3, and claims 4-5 by dependency, are rejected under 35 U.S.C. 103(a) as being unpatentable over Janusz et al. (US 2005/0152985) in view of Cancer Principles (Cancer Principles & Practice of Oncology, 6th Ed., De Vita et al., eds., Lippincott Williams & Wilkins, Philadelphia, 2001, pp. 308-312). Janusz et al. disclose that

mammalian colostrum contains the polypeptide colostrinin, which has a number of biological activities, including stimulating the release of cytokines from lymphocytes (see paragraphs 1-3, 6, 7 and 44-47). Colostrinin is present in the colostrum of sheep and humans and is itself a cytokine (see paragraphs 3, 6 and 44). Colostrinin may be used to treat humans (see paragraph 6). Cytokines have anti-cancer properties and are administered to cancer patients (see Cancer Principles & Practice of Oncology, 6th Ed., De Vita et al., eds., Lippincott Williams & Wilkins, Philadelphia, 2001, pp. 308-312, especially the 1st full paragraph on p. 312). Thus, it was known at the time of Applicant's invention that colostrum contains at least one substance that has anti-cancer properties. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to obtain an anti-tumor substance from colostrum, because Janusz et al. disclose that colostrum contains a polypeptide that is a cytokine and that stimulates the release of cytokines from lymphocytes and because Cancer Principles discloses that cytokines have anti-tumor properties.

Although Janusz et al. do not disclose using colostrum from even-toed hoofed animals with leukosis as a starting material, they disclose using colostrum from healthy even-toed hoofed animals, sheep in particular. One of ordinary skill in the art would have expected the colostrum of even-toed hoofed animals to contain a substance having anti-cancer properties whether or not the animal has leukosis, because the anti-cancer substance is naturally produced in the animal's colostrum whether or not the animal has leukosis. The substance is not produced in response to an agent that causes the leukosis.

In view of the foregoing, a holding of obviousness is required.

No claim is allowed.

Regarding Applicant's proposed amendment that was transmitted to the public fax number on December 23, 2005, these claims have not been entered, searched or examined because they were not added by preliminary amendment. Moreover, they are directed to a non-elected invention, a method of preparing an antibody. Such an invention is not examined in this art unit or this work group (the 1650s), and it would require transfer to the proper art unit. Amended claims must read on the elected invention.

Additionally, Applicant should note that there is no statement in the specification that the anti-tumor substance in colostrum is an antibody. The specification merely states that newborns benefit from receiving colostrum because it contains a concentrated amount of antibodies that help newborns fight infection. Secondly, Applicant has attempted to broaden the elected method claims with steps in claim 4, and various dependent claims, that recite using any alcohol and any solvent in any ratio, with or without centrifugation, to isolate an antibody with anti-tumor properties. The specification discloses only one method for isolating an undefined anti-tumor substance from colostrum, using one defined set of solvent mixtures and centrifugation parameters. This method is disclosed on the bottom of p. 2 and the top of p. 3.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rosanne Kosson
Examiner, Art Unit 1653

rk/2006-01-04

ROBERT A. WAX
PRIMARY EXAMINER